UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA

THE CITY OF HUNTINGTON, Plaintiff, v. AMERISOUCEBERGEN DRUG CORPORATION, *et al.* Defendants	Civil Action No. 3:17-01362
CABELL COUNTY COMMISSION, Plaintiff, v. AMERISOUCEBERGEN DRUG CORPORATION, *et al.* Defendants	

PLAINTIFFS' MEMORANDUM IN OPPOSITION TO MOTION TO EXCLUDE TESTIMONY OF KATHERINE KEYES, PH.D.

November 12, 2020

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INTRODUCTION

Defendants seek to preclude Dr. Katherine Keyes from offering her computation of overdose deaths in Cabell County "directly" attributable to prescription opioids, her computation of the rate of "opioid use disorder" or "OUD" in Cabell County, and her explanations of either computation. *See* Expert App'x, Dkt. # 1097, at Exh. 5.a, at 33-45, 48-50 (Keyes Rpt.) (deaths directly attributable to prescription opioids); *id.* at 41-42 (Cabell County OUD rate calculation); *see also* Expert App'x, Dkt. # 1097, at Exh. 5.d (Aug. 24, 2020 Errata) (correcting Keyes Rpt. at 50 fig. 16); Expert App'x, Dkt. # 1097, at Exh. 5.e (Sept. 23, 2020 Errata) (correcting data underlying of Keyes Rpt. at 48-50). Defendants' motion should be denied in its entirety.[1]

Defendants do not challenge Dr. Keyes' qualifications, nor could they, as she is a highly-credentialed, much-published epidemiologist with specific expertise (predating this litigation) in the opioid epidemic. *See* Expert App'x, Dkt. # 1097, at Exh. 5.a, at 4-6 (Keyes Rpt.). Nor do they challenge any of the 13 identified opinions disclosed in Dr. Keyes' report. *See id.* 6-7. The two computations Defendants do seek to exclude are reliable, methodologically sound, and admissible. The technical disagreements reflected in Defendants' motion are beyond the scope of a Rule 702 motion. That rule does not authorize second-guessing the judgments of a qualified epidemiologist applying standard and accepted epidemiological methods. The Court need not and should not decide whether Dr. Keyes' computations are correct in order to conclude that they are admissible.

[1] In an effort to provide a complete record, the parties agreed, and the Court approved, a delay of the deadline within which to file this Opposition to allow the parties to proceed with a limited, supplemental deposition of Dr. Keyes. In addition, the parties agreed to a modest page extension of the applicable page limits.

THE KEYES REPORT AND THE TESTIMONY AT ISSUE

Dr. Katherine Keyes is an Associate Professor of Epidemiology at Columbia University, specializing in substance use and substance use disorders epidemiology. Expert App'x, Dkt. # 1097, at Exh. 5.a, at 11 (Keyes Rpt.). Epidemiology is the "science of understanding the causes and distributions of population health" and "epidemiologists examine the dynamic nature of populations and how health and disease arises within them." Dr. Keyes has extensive expertise with respect to opioid-related harm. She is a faculty member of the Policy and Health Initiatives on Opioids and Other Substances Center at Columbia University and a steering committee member of the Substance Abuse Epidemiology Training Programs, through which she trains and mentors doctoral and post-doctoral scholars in substance abuse epidemiology. *Id.* Dr. Keyes also is an investigator on the HEALing Committees Study, a large, $350 million dollar NIH grant-funded initiative aiming to reduce opioid overdose by 40 percent in four states, including New York, Ohio, Kentucky, and Massachusetts. She has published 21 peer-reviewed journal articles on opioid use and related harms (and many more on drug use disorders generally).[2]

On August 3, 2020, Plaintiffs provided Defendants a 54-page expert report for Dr. Keyes ("Report"). *See* Expert App'x, Dkt. # 1097, at Exh. 5.a. (Keyes Rpt.). On August 24, 2020, Plaintiffs provided Defendants with an errata to the Report correcting certain errors in the original. *See* Expert App'x, Dkt. # 1097, at Exh. 5.d (Aug. 24, 2020 Errata). On September 15, 2020, Defendants took Dr. Keyes' deposition. On September 23, 2020, Plaintiffs provided a second errata correcting certain data and computations in the Report. *See* Expert App'x, Dkt. # 1097, at Exh. 5.e. (Sept. 23, 2020 Errata). After Defendants served their motion to exclude the two computations at issue, the parties agreed that Dr. Keyes would sit for a three-hour

[2] *See, e.g.*, Exh. A, M. Cerda, *et al*., *Prescription Opioid Mortality Trends in NYC, 1990-2006*, 132 DRUG ALCOHOL DEPENDENCY 1-21, 10 (2013).

supplemental deposition, with broad latitude for questioning on both errata, as well as on previously served calculations, and "the effect her changed calculations have on her opinions as a whole." Ex. B, Email from Metz to do Amaral, 10/21/20. The deposition was held on October 30, 2020. The contents of the corrected Report and the substance of Dr. Keyes' deposition testimony are discussed as relevant below.

In her Report, Dr. Keyes offers opinions about the rise in medical and non-medical use of prescription opioids; the correlation between increases in supply of such drugs and increases in non-medical use and in harms associated with such use; the relationship between increased use of prescription opioids and increased use of heroin; increases throughout the United States, and specifically in the Cabell-Huntington community, in OUD, overdose deaths from opioids, and other harms. Expert App'x, Dkt. # 1097, at Exh. 5.a, at 6-7 (Keyes Rpt.). Defendants do not challenge any of these opinions in this motion.[3] Defendants challenge only the two computations identified above. Notably, while Defendants seek to preclude Dr. Keyes from presenting these computations, they do *not* seek to preclude her from offering any opinions based on them. Defendants' motion is, accordingly, quite narrow and affects only the extent to which Dr. Keyes may, in her testimony, reference these two particular computations in explaining and supporting her opinions.[4]

[3] Defendants have filed a separate motion seeking to exclude certain opinions offered by Dr. Keyes and others pertaining to the causal connection between marketing activities and increased availability of prescription opioids. Plaintiffs address that challenge in their separate opposition to that motion. This memorandum pertains only to Defendants' challenges to the two computations described in the text.

[4] Defendants recognize that Plaintiffs' economics and abatement experts, Profs. Thomas McGuire and Caleb Alexander, made use of Dr. Keyes' computations in forming their opinions. *See* Def. Mem. at 3-4. However, although Defendants seek to preclude both of these experts from testifying altogether, their challenges do not in any way depend on, or reference, the use of Dr. Keyes' computations. Defendants do not contend that the opinions of these experts are in any way unreliable because of their use of Dr. Keyes' work.

Dr. Keyes' Computations Pertaining to Fentanyl Overdose Deaths

The first computation Defendants challenge pertains to the number of overdose deaths that can be attributed to prescription opioids. Dr. Keyes based her analysis on data from the National Vital Statistics Surveillance System (NVSS), which "provides publicly available county-level data on death, allowing for a quantification of the risk of overdose death in Cabell County." Expert App'x, Dkt. # 1097, at Exh. 5.a, at 31 (Keyes Rpt.). The NVSS receives and analyzes data from death certificates, including cause-of-death information reported by medical examiners and coroners.[5] Dr. Keyes reviewed this data for Cabell County focusing on specific codes (referred to as "ICD codes") used in death certificates to identify the particular drugs involved in overdose deaths. *See id.* at 33. Noting that death certificates may list more than one drug, Dr. Keyes explains the significance of drug-drug interactions, and the basis, in the scientific literature, for treating all overdose deaths for which a prescription opioid is listed on the death certificate as having been caused in part by that drug. *Id.* at 37.

In her analysis of opioid overdose deaths, Dr. Keyes computed both overdose deaths caused "directly" by prescription opioids—those "for which prescription opioids were listed as a contributing factor on the death certificate"—and overdose deaths caused "indirectly" by prescription opioids, defined by Dr. Keyes as "opioid deaths for which prescription opioids were not listed on the death certificate, but that we can conservatively estimate can be attributed to the initiation of opioid use with prescription opioids." *Id.* at 49. As the Report explains, "[p]rescription opioid use is . . . causally related to the increase in synthetic opioid[6] morbidity and mortality, since prescription opioids frequently precede the transition to heroin, including

[5] *See* Centers for Disease Control and Prevention, https://www.cdc.gov/nchs/nvss/drug-overdose-deaths.htm (last visited Nov. 12, 2020).

[6] Synthetic opioids include fentanyl.

heroin contaminated with fentanyl." *Id.* at 6. Indeed, studies show that "70-80% of individuals who use heroin and other opioids also used prescription opioids prior to the start of heroin and other opioid use." *Id.* at 49. Thus, "heroin and fentanyl deaths are a result of the increase in prescription opioid use in the United States to the extent that prescription opioid use is concurrent with, or temporally prior and causally related to subsequent heroin and fentanyl use." *Id.* at 32. For this reason, computing only the overdose deaths for which prescription opioids were listed as a contributing factor on the death certificate would dramatically understate the number of overdose deaths that were actually caused by increases in the supply of prescription opioids.

Fentanyl is found in both prescription and illicit form, but death certificate codes do not differentiate between the two. "Available evidence from the CDC indicate that in approximately 2013-2015, illegally manufactured fentanyl began to be detected in illicit drug supply, leading to exponential increases in overdose death." *Id.* at 33. Because there was virtually no illicit fentanyl available in the United States before 2013, Dr. Keyes counted all deaths attributed to fentanyl before 2013 as directly attributable to prescription opioids. See *id.* ("common" practice before 2013 was to code synthetic opioid death as prescription opioid death). For the period after 2013—that is, after the introduction of illicit fentanyl—Dr. Keyes's Second Errata[7] conservatively estimated the percentage of the total fentanyl deaths caused by prescription fentanyl by averaging synthetic opioid overdose deaths per year from 1999 to 2012 and carrying that average forward from 2013 onwards as the number of prescription synthetic opioid overdose deaths. Holding the number of deaths from prescription fentanyl constant, Dr. Keyes judged that

[7] The Report originally used a different metric, which Defendants do not challenge. Expert App'x, Dkt. # 1097, at Exh. 5.a, at 33 (Keyes Rpt.).

all of the increases in fentanyl deaths after 2012 were caused by illicit fentanyl and thus only indirectly attributable, if at all, to Defendants' conduct.

Dr. Keyes further adjusted her computation to reflect that only a portion of the deaths from heroin and illicit fentanyl arose from prior use of prescription opioids. For the year 2017, for example, Dr. Keyes found 27 deaths directly attributable to prescription opioids, based on death certificate coding adjusted for differentiating prescription fentanyl from illicit fentanyl. She found an additional 105 deaths attributable to non-prescription opioids, based on death certificate coding adjusted for differentiating prescription fentanyl from illicit fentanyl. Of those 105 non-prescription opioid deaths, she found that 56 could be indirectly attributed to prescription drugs, for the reasons explained above. Thus, she determined that, in 2017, the total number of opioid overdose deaths attributable, directly or indirectly, to prescription opioids was 27 + 56 for a total of 83. *See* Expert App'x, Dkt. # 1097, at Exh. 5.e (Sept. 23, 2020 Errata). Dr. Keyes made similar computations for each year from 2006 to 2018.

Dr. Keyes' Computation of OUD in the Cabell-Huntington Area

The second computation Defendants challenge is Keyes's estimate of "the number of individuals with opioid use disorder (OUD) in . . . Cabell County in order to obtain an estimate of the number who should have access to services to treat OUD." Expert App'x, Dkt. # 1097, at Exh. 5.a, at 41 (Keyes Rpt.) As Dr. Keyes explained:

> A well-accepted method in epidemiology for many years for estimating population sizes for difficult to count groups [is] to use multiplier methods: divide the known rate of an outcome for the difficult to count group by the number of individuals in the population of interest with the outcome to estimate the size of the difficult to count group. For individuals with OUD, available systematic review and meta-analyses have estimated the overdose mortality rate of individuals who are ascertained as having OUD, in treatment for OUD, or otherwise can be reasonably assumed to experience OUD based on duration and extent of opioid use.

Id. at 42. Put another way, if it is known that one in 100 persons with a condition will die of it, and if there are 20 deaths, we can estimate that there are a total of 2,000 people with the condition. Here, because the number of opioid overdose deaths is readily available and the percentage of individuals with OUD who die of opioid overdose has been reliably estimated, the number of individuals with OUD can be estimated.

In support of this approach, Dr. Keyes cited numerous studies showing that, "among 'extramedical' opioid users," the "estimated overdose death rate . . . was 0.52 per 100 person-years." *Id.* Dr. Keyes noted that the underlying studies that were analyzed to produce this estimate were published before the appearance of drugs adulterated with fentanyl, and thus before the outbreak of illicit fentanyl-induced deaths. As she explained, "the estimated overdose event rate from synthetic opioid use is approximately three times that of heroin based on available literature. . . ." *Id.* For this reason, Dr. Keyes judged it appropriate to apply a correction to the 0.52 per 100,000 death rate, to account for the higher mortality rate associated with fentanyl adulteration. Accordingly, Dr. Keyes estimated the number of Cabell County OUD cases by applying a 0.52 per 100,000 death rate to the 16% of overdose deaths in Cabell County caused by opioids other than synthetic opioids, and a death rate three times higher, 1.56 per 100,000, to the 84% of overdose deaths in the County from illicit synthetic opioids. *Id.* at 42-43.

LEGAL STANDARD

Plaintiffs respectfully refer the Court to the Legal Standard set forth in Plaintiffs' Memorandum in Opposition to Defendants' Motion to Exclude the Expert Testimony of Andrew Kolodny, Dkt. # 1099, at 4-7, incorporated herein by reference.

ARGUMENT

I. DR. KEYES APPLIED GENERALLY ACCEPTED METHODS TO STATE THE NUMBER OF DEATHS DIRECTLY AND INDIRECTLY ATTRIBUTABLE TO PRESCRIPTION OPIOIDS.

Defendants make two arguments in support of their argument that Dr. Keyes's estimate of the number of deaths directly and indirectly attributable to prescription opioids should be excluded. First, Defendants contend that Dr. Keyes improperly classified deaths involving more than one drug. Second, Defendants argue that Dr. Keyes did not disclose the methodology she used to distinguish deaths from prescription fentanyl from deaths from illicit fentanyl. Neither argument justifies excluding this computation.

A. Dr. Keyes Properly Analyzed Deaths Involving More Than One Drug

1. Generally accepted methodology attributes cause of death to each drug, where there are multiple opioids identified on autopsy.

Defendants criticize Dr. Keyes' "direct" attribution of deaths to prescription opioids when a death certificate listed both a prescription opioid as well as another drug, arguing that Dr. Keyes "begins by reclassifying deaths caused at least in part by illicit fentanyl or heroin as deaths caused by prescription opioids *alone*."[8] Nowhere in her Report or testimony did Dr. Keyes "reclassify" any deaths or describe such deaths as having been caused by prescription opioids "alone." Instead, Dr. Keyes' adhered to standard practice in the field of epidemiology, which attributes death to *each* identified drug in these circumstances.

As Dr. Keyes testified, epidemiologists treat death certificate codes as a reliable judgment, "[u]sually" a medical examiner's, that the drugs coded were "contributing causes" of the death. Ex. C, Keyes Dep. 185:8, 187:21 (Sept. 15, 2020). "The definition of 'cause' is a factor without which the outcome would not have occurred": what lawyers call a but-for cause and logicians call a necessary condition. *Id.* at 190:14-15. "So there could be multiple causes" in

[8] Def. Mem. at 4 (emphasis in original).

this sense. *Id.* at 190:17; *see also id.* at 190:23-191:9 (codes represent medical examiner's judgment of death's necessary conditions); Expert App'x, Dkt. # 1097, at Exh. 5.a, at 37 (Keyes Rpt.) (citing "substantial epidemiological, toxicological, and clinical literature" on implications of polydrug use for causal attribution).

The death certificate data Dr. Keyes relied on are published by the United States Centers for Disease Control (CDC), the recognized authority on the subject of drug death classification, providing reliable and widely used data on overdose deaths. Ex. C, Keyes Dep. 184:20. Consistent with Keyes's understanding, the CDC data recognize that "drug overdose deaths may involve multiple drugs; therefore, *a single death might be included in more than one category when describing the rate of drug overdose deaths involving specific drugs.* For example, a death that involved both fentanyl and cocaine would be included in both the rate of drug overdose deaths involving synthetic opioids other than methadone and the rate of drug overdose deaths involving cocaine."[9] *Accord, e.g.*, Expert App'x, Dkt. # 1097, at Exh. 5.a, at 32 (Keyes Rpt.) ("Figure 4 provides the number of drug overdose deaths in West Virginia across three categories . . . . These categories are not mutually exclusive; deaths for which more than one drug was listed were counted in each category; thus the category totals represent counts of events of drugs, and do not sum to the total number of deaths.").[10]

In short, Defendants are wrong to claim that Dr. Keyes "re-classified" anything. Dr. Keyes took the CDC data as she found them. The CDC in turn took the medical examiners'

[9] *Drug Overdose Deaths in the United States*, 1999–2018; National Center for Health Statistics (NCHS) Data Brief No. 356, Jan. 2020 (*available at* https://www.cdc.gov/nchs/products/databriefs/db356.htm) (emphasis added).

[10] In order to avoid counting each death multiple times, Dr. Keyes' analysis counted each death in which a prescription drug was present as a death directly attributable to prescription opioids. She then computed a fraction of the remainder of the deaths that should be treated as indirectly attributable to prescription opioids. Deaths already counted as directly attributable were thus not also counted as indirectly attributable, even though both types of drugs may have been present.

multiple causal determinations as it found them. This is standard epidemiological practice; neither a "medical degree" nor "experience as a medical examiner" was required. Further, Dr. Keyes explains why multiple causation is particularly likely in opioid-involved deaths:

> When multiple drugs are listed as part of the contributing causes of death in an overdose death, the preponderance of evidence indicates that certain combinations of drugs, especially those that include opioids, are associated with multiplicative increases in risk of death; that is, without the prescription opioid, *the individual would not have died when and how they did*.

Expert App'x, Dkt. # 1097, at Exh. 5.a, at 7 (Keyes Rpt.) (emphasis added). Defendants do not challenge the admissibility of this opinion. Yet it is precisely this opinion that explains why Dr. Keyes' methodology is sound and why it is appropriate for Dr. Keyes to treat all deaths in which a prescription opioid is listed on the death certificate as a death "directly attributable" to prescription opioids.

2. Dr. Keyes' categories of deaths "directly attributable" and "indirectly attributable" to prescription opioids are based on reliable methodology and peer-reviewed literature.

Defendants argue that a death cannot be "directly" attributable to prescription opioids when an illicit opioid such as fentanyl is also identified on a death certificate.[11] They are wrong. As Dr. Keyes' Report explains,[12] the CDC methodology described above prescribes that deaths are considered "directly" attributable to prescription opioids in all cases where a prescription opioid was identified as a cause of death The presence of an additional drug does not change that direct relationship to a prescription opioid. If a prescription opioid and another drug are both identified as causes of death, then both are "directly" related to the death.

[11] Def. Mem. at 4-5.

[12] Expert App'x, Dkt. # 1097, at Exh. 5.a, at 4-50 (Keyes Rpt.) (explaining method for "direct" and "indirect" attribution); *see also id.* at 37 (explaining "implications for causal attribution" of "multiple drugs listed on death certificates").

The category of deaths "indirectly" attributable to prescription opioids is likewise based on the evidence and the peer-reviewed literature. Dr. Keyes defined "[d]eaths indirectly attributable to prescription opioids" as "deaths for which prescription opioids were not listed on the death certificate, but that we can conservatively estimate can be attributed to the initiation of opioid use with prescription opioids."[13] This simply recognizes that, as is well documented in the literature, many individuals who begin abusing prescription opioids will eventually transition to using illicit opioids; the prescription opioids are the initiating cause regardless of which drug is found in the body after an overdose death. Since the beginning of the prescription opioid epidemic in the late 1990s, the medical literature reports that 70-80% of illicit opiate users began their opioid dependence with prescription opioids.[14] Dr. Keyes applied a more conservative figure based on data from the National Survey of Drug Use in Households (NSDUH),[15] which reported that an average of approximately 53% of illicit opioid users began with prescription opioids. Accordingly, Dr. Keyes opined that 53% of illicit opiate deaths were "indirectly" attributable to prescription opioids – that is, the death would not have occurred if not for the prior, initiating use of prescription opioids, even if the immediate precipitating cause of death was an illicit opioid [16] These opinions were based on application of principles and findings from peer-reviewed literature to the best available drug mortality statistics. Dr. Keyes applied a reliable methodology to determine the proportion of deaths that were directly and indirectly attributable to prescription opioids.

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[13] *Id.*

[14] *Id.*

[15] *Id.* at 50.

[16] *Id.* at 51.

3. Dr. Keyes' Use of an Estimate to Replace Missing Data Does Not Render Her Methodology Unreliable

Although Defendants' motion does not challenge the estimate that Dr. Keyes used to replace certain missing data used in this computation, Plaintiffs anticipate that they may do so in reply. As discussed above, Dr. Keyes used data from the CDC to perform her computations pertaining to overdose deaths. When a particular locale reports fewer than 10 overdose deaths during a particular period, it is CDC policy not to report any number at all.[17] For these "suppressed" values, Dr. Keyes treated the missing number as five, the midpoint between zero and ten, the highest and lowest values eligible for suppression.[18] Dr. Keyes used actual data in the years for which it was available, and the midpoint estimate in the years when it wasn't, to estimate that from 1999 to 2012 there were three deaths per year due to prescription fentanyl. She estimated further that, after the introduction of illicit fentanyl in 2013, growth in the number of annual deaths was attributable to illicit fentanyl, so that the number of deaths directly attributable to prescription fentanyl remained at a constant three per year.

Plaintiffs anticipate Defendants will argue that the use of the mid-point estimate resulted in higher estimates of deaths attributable to prescription fentanyl than would have resulted from use of actual data. This argument should be rejected. As Dr. Keyes explained, while the estimate of five prescription fentanyl deaths was higher than the average of actual known values for some years, for others, it was lower, and "[t]hat's kind of how math works."[19]

The use of the mid-point estimate for years when data was missing produced an overall figure for prescription fentanyl deaths entirely consistent with other known data. There were 25

[17] Exh. D, Keyes Dep. 74:14-20 (Oct. 30, 2020). This policy is intended to protect privacy when small numbers would allow identities of overdose victims to be discerned. *Id*

[18] *Id.* 75:2-19.

[19] *Id.* 100:8-9; *see also id.* at 109:12-14 ("replacing it with a mean value is a very commonly used method").

prescription fentanyl deaths in Cabell County in the eight years for which actual data were available from the CDC WONDER data set between 1999-2012, for an average of 3.1 per year; that figure is essentially identical to the figure of three deaths per year estimated by Dr. Keyes.[20] The reliability of Dr. Keyes' estimate is also supported by Plaintiffs' expert witness Gordon Smith, M.B., Ch. B., who used local Cabell County overdose data *not* subject to CDC data suppression policies. From 2001 to 2013, Dr. Smith found 44 fentanyl deaths, for an average of 3.67 deaths per year.[21] Dr. Keyes' use of estimated values, where data had been suppressed, resulted in a reasonable, conservative, and somewhat lower estimate of prescription fentanyl deaths than shown in the local, non-suppressed data.

4. Defendants' Attacks on Dr. Keyes' Original Computation Provide No Basis to Exclude Her Opinion

Defendants seek to bolster their challenge to the computation Dr. Keyes proposes to offer by attacking an earlier computation that Dr. Keyes has since corrected. Even if that original computation were flawed—and Plaintiffs do not concede that it was—that would not demonstrate any methodological flaw Dr. Keyes *current* methodology. Defendants rely on a misleading excerpt of Dr. Keyes' deposition transcript to claim that she did not understand the methodology she originally used to calculate deaths directly attributable to prescription fentanyl during the years 2014-2018, when illicit fentanyl became widely available.[22] The full transcript shows, instead, that Dr. Keyes was unable to answer a question based on a data spreadsheet that defense counsel had failed to provide. As part of the same answer that was excerpted in the Defendants' brief, Dr. Keyes explained, "I performed a lot of analyses to come up with these

[20] *Id.* 105:1-106:4.

[21] Expert App'x, Dkt. # 1097, at Exh. 12.a, at 9-10, and *Id.* at 12.b. (Smith Rpt.).

[22] Def. Mem. at 9 nn.18-19.

estimates, and *I would need to see specifically what you're referring to*."[23] Defense counsel did not provide the spreadsheet in advance of the deposition, contrary to the Court-ordered protocol.[24] When defense counsel asked whether Dr. Keyes had a "working knowledge" of the data and calculations in the spreadsheet, she testified that she did, and she then described the methodology that she had followed.[25] Moreover, the questioning to which Defendants point related to the actual computations and the use of an Excel spreadsheet to perform them. It did not pertain to the methodology for determining the proper percentage of fentanyl deaths to treat as directly attributable to prescription fentanyl. On that subject, Dr. Keyes answered numerous questions about her methodology, and displayed a clear and deep understanding of the reason for using the metric she used. *See* Ex. C, Keyes Dep. 342:14-366. Even if Defendants sought to exclude Dr. Keyes' testimony on this basis—and it does not appear that they have—their false claim that Dr. Keyes did not understand her own methodology should be rejected.

B. Dr. Keyes' Analysis Should Not Be Excluded as a Discovery Sanction

Defendants also argue that Dr. Keyes' computation should be excluded because Plaintiffs failed timely to disclose the methodology she used to determine the number of overdose deaths directly and indirectly attributed to fentanyl. Defendants inaccurately allege that Dr. Keyes revised her opinions "several" times,[26] when in fact there was only a single substantive revision, preceded by a non-substantive correction of data that were inadvertently included in the Keyes

[23] Exh. C, Keyes Dep. 340:12-14 (emphasis added).

[24] *Id.* at 340:15-19 (Defense counsel "wasn't aware until today" that the relevant spreadsheet had not been sent out with the set of deposition exhibits).

[25] *Id.* at 342:10-343:14.

[26] Def. Mem. at 7.

Report of August 3, 2020.[27] The single substantive revision is Dr. Keyes' Second Errata, which was served on September 23, 2020.

Significantly, Defendants do not suggest that the methodology Dr. Keyes used in the Second Errata is unreliable, only that Dr. Keyes failed timely to disclose it.[28] They seek exclusion purely as a Rule 37 discovery sanction. No such sanction is warranted here.

Rule 37(c)(1) governs the imposition of sanctions, including preclusion, for failure to comply with discovery obligations. The rule does not authorize exclusion of expert witness testimony "if the non-compliance was substantially justified or harmless." Fed. R. Civ. P. 37(c)(1). "The Fourth Circuit has held that a district court has broad discretion to determine whether a nondisclosure of evidence is substantially justified or harmless for purposes of a Rule 37(c)(1) exclusion analysis." *Goldman v. Phillips & Son Drilling, Inc. et al*, Civil No. 3:13-CV-152, 2014 WL 3407066 at 2. (N.D. W.Va. July 10, 2014) (internal quotation marks omitted). Most courts in similar situations have permitted a non-compliant party an opportunity to provide

[27] As Defendants acknowledge in their Memorandum, the Keyes Report of August 3 included a description of the method for estimating deaths "directly" and "indirectly" attributable to prescription opioids, after the increased prevalence of illicit fentanyl after 2013 (as opposed to prescription fentanyl, which had been available from the 1990s onward). *Id.* at 7-8. However, Defendants fail to inform the Court that they had been made aware, almost two months ago, that *the results of that analysis were mistakenly omitted from the August 3 Report*. Instead, due to "inadvertent inclusion of a nonfinal figure," Exh. E, McGuire Dep. 116:16-121:10 (Sept. 9, 2020), Figure 16 of the Keyes Report included data that differed from the results of the analysis described in the Report. Defendants were first provided with the correct data for Figure 16 on August 13, 2020, when Plaintiffs provided a spreadsheet of the data for all of Dr. Keyes' figures, in response to a request from defense counsel. *See* Expert App'x, Dkt. # 1097, at Exh.5.c (Aug. 13, 2020 email transmitting input calculations). On August 24, 2020, Plaintiffs served an errata that displayed the data previously provided on August 13, and also produced a revised Figure 16 that matched the results of the analysis set forth in the August 3 Report. *See* Expert App'x, Dkt. # 1097, at Exh. 5.d (Aug. 24, 2020 Errata).

[28] If Defendants believed that carrying forward the constant number of three prescription fentanyl deaths per year was methodologically flawed or unreliable in any way, they would have said so in their opening memorandum. That memorandum makes clear that, even before Dr. Keyes' supplemental deposition, Defendants were well aware that the Second Errata applied a constant rate of three fentanyl deaths per year. Def. Mem. at 9.

the required information rather than to strike the testimony. *See, e.g.*, *Watkins v. Cook Inc.*, Civil Action No. 2:13-cv-20370, 2015 WL 1395773, at 22-23 (S.D. W.Va. March 25, 2015); *Ace American Ins. Co. v. McDonald's Corp.*, Civil Action No. GLR-11-3150, 2012 WL 2523883, at 5 (D. Md. June 28, 2012); *Kristensen ex rel. Kristensen v. Spotnitz*, Civil Action No. 3:09-CV-00084, 2011 WL 5320686, at 4 (W.D. Va. June 3, 2011); *Kobe v. Haley*, C/A No. 3:11-1146, 2013 WL 4067921, at 5 (D.S.C. Aug. 12, 2013).

Here, any delay in providing Dr. Keyes Second Errata was both substantially justified and harmless. Rule 26(e) requires that a party serve a supplemental disclosure if it learns that its prior disclosure is incomplete or incorrect. *See also* Fed. R. Civ. P. 26(a)(2)(E) (requiring supplementation of expert disclosures). Defendants do not suggest that Plaintiffs delayed in any way in providing Dr. Keyes' corrections to her prior disclosures. The Second Errata was served promptly once Dr. Keyes determined that a more conservative approach would be appropriate in the particular circumstances of this case.

Nor can there be any prejudice whatsoever because Defendants have had the opportunity to depose Dr. Keyes after receiving the Second Errata. As noted above, Plaintiffs served the Second Errata on September 23, 2020. *See* Expert App'x, Dkt. # 1097, at Exh. 5.e (Sept. 23, 2020 Errata). After receiving Defendants' motion on October 2, 2020, Plaintiffs offered to produce Dr. Keyes for an additional deposition for the specific purpose of inquiring about the basis and methodology of the errata served following the initial deposition of September 15, 2020, as well as the sequence of reports and opinions.[29] Defendants agreed and the deposition took place on October 30. Defendants have had a full opportunity to question Dr. Keyes about

[29] Exh. B, Email from Metz to do Amaral, 10/21/20. Plaintiffs note that between the time Defendants received the Second Errata and the time they filed their motion, Defendants could have asked for the opportunity to re-depose Dr. Keyes. Instead, they simply filed their motion seeking preclusion without attempting to attain the discovery they argue was needed.

her revised computations. Thus, even if the timing of the Second Errata could ever have prejudiced the Defendants, the supplemental deposition has cured any possible prejudice.

Good evidence of the absence of prejudice is the fact Defendants did not use the supplemental deposition to inquire about the Second Errata. Rather, as discussed above, they devoted much of the deposition to inquiring about the use of the midpoint to replace missing data. If the timing of the Second Errata had truly prejudiced Defendants by depriving them of the opportunity to ask Dr. Keyes about it at deposition, they would have asked those questions on October 30. They did not. Without any conceivable prejudice from the timing of the Second Errata, there can be no basis for the harshest sanction of exclusion.

Defendants may argue that Dr. Keyes also failed timely to disclose her missing data estimate. Not so. On August 13, 2020 (*see* Expert App'x, Dkt. # 1097, at Exh. 5.c), Dr. Keyes responded to Defendants' request for the calculations that supported the Report. Her response explicitly informed Defendants, "deaths have been set to 5, *as this is the midpoint in the range of possible suppression values.*"[30] This was a sufficient disclosure of the simple methodology applied to suppressed values, a method that Dr. Keyes' testified has been "commonly used" for "the last hundred years of epidemiology."[31] Defendants had the August 13, 2020 worksheets for over a month before Dr. Keyes' initial deposition on September 15, 2020, when they had a full opportunity to inquire about the use of estimates in place of suppressed values. They have since had a second opportunity to inquire about this portion of Dr. Keyes' methodology.

Finally, the Second Errata affected only the categorization of deaths "indirectly attributable" to prescription opioids for the years 2013-2018. Even if the Court were to find a discovery sanction appropriate —and it should not—any relief it should be limited to the post-

[30]Exh. F, Keyes Dep., Exh. 10 (Oct. 30, 2020) (emphasis added).

[31]Exh. D, Keyes Dep. 110:11–12.

2013 analysis of mortality indirectly attributable to prescription opioids. No other computations or opinions are affected.

II. DR. KEYES' ESTIMATE OF OUD IN CABELL COUNTY IS RELIABLE AND SUPPORTED BY ACTUAL OUD CASE COUNTS AND COMMUNITY STATEMENTS.

The second computation Defendants challenge is Dr. Keyes' estimate of the number of people in Cabell County with OUD. To estimate the OUD population, Dr. Keyes applied a well-recognized method based on peer-reviewed literature and actual population data, to estimate that between 8,186 and 8,309 individuals in Cabell County have OUD.[32] Dr. Keyes' Report states that it is "well-accepted" in epidemiology to estimate the population sizes for a difficult to count group by "multiplier methods: divide the known rate of an outcome for the difficult to count group by the number of individuals in the population of interest with the outcome to estimate the size of the difficult to count group."[33] Dr. Keyes further states that "the present methodology, using available literature estimates to extrapolate to population sizes, is one that I have used in numerous studies that are published in peer-reviewed journals."[34]

Defendants do not challenge Dr. Keyes' relevant qualifications, nor the legitimacy of the multiplier method. Instead, they attack the means by which Dr. Keyes applied this well-accepted methodology. They argue that the conditions necessary to use the multiplier method were not present, and that Dr. Keyes failed to account for the most recent data in applying the method. Neither is true.

[32] Expert App'x, Dkt. # 1097, at Exh. 5.a, at 42-43 (Keyes Rpt.).

[33] *Id*. at 41.

[34] *Id.* at 44.

A. Dr. Keyes Properly Applied the Multiplier Method

Defendants rely on a lawyer's reading of a textbook chapter in epidemiology to claim that Dr. Keyes did not adhere to the standards for application of the multiplier method.[35] Defendants first argue that Dr. Keyes' use of the multiplier method is deficient because the rate of opioid mortality varied from year to year, such that the method did not meet the criterion of a "stable population."[36] However, the textbook cited by Defendants states that population "stability" refers to the "number of drug users entering or exiting the population," and *not* whether the mortality rate changes from year to year.[37] Defendants' argument is thus based on an inaccurate reading of the text on which they rely.

Defendants next claim that Dr. Keyes failed to identify a complete and accurate "benchmark" population because the meta-analysis that she used for the benchmark mortality rate included studies of non-fentanyl drugs.[38] This argument ignores the fact that Dr. Keyes made an explicit adjustment of the benchmark mortality rate to account for the greater toxicity of fentanyl.

In addition, the textbook Defendants cite states that results based on the multiplier method should be cross-checked against other sources.[39] Dr. Keyes met this criterion by including cross checks of the estimates of the OUD prevalence in Cabell County/Huntington. In particular, Dr. Keyes' OUD estimate based on the multiplier method was closely matched by the

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[35] *Id.* at 16-19.

[36] *Id.* at 16-17 (citing Exh. G, Hickman M., Taylor C. *Indirect Methods to Estimate Prevalence*. In: Sloboda Z. (eds) EPIDEMIOLOGY OF DRUG ABUSE. Springer, Boston, MA. https://doi.org/10.1007/0-387-24416-6_8 (2005)).

[37] Exh. G, Hickman and Taylor, at 118.

[38] Def. Mem. at 17-18.

[39] Exh. G, Hickman and Taylor, at 122.

real-world OUD diagnoses in Cabell County/Huntington provided by Dr. Todd Davies, based on actual counts from local hospitals and clinics.[40]

Finally, the Court may take into account that Dr. Keyes has published repeatedly using the multiplier method and has studied and published on substance use disorders, and specifically on prescription and illicit opioids, throughout her career.[41] In contrast, the expert relied upon by Defendants to criticize Dr. Keyes' analysis, Rahilly-Tierney, has not authored any peer-reviewed publications that focused on opioid medications, OUD, substance use disorder, or polysubstance abuse disorder; she has never presented formal instruction, in a classroom or in a formal presentation, on the topic of opioid medication; and, although she claims an affiliation with Harvard Medical School, she is not, in fact, employed in any form or fashion by Harvard Medical School.[42] Dr. Keyes has the relevant expertise to apply the multiplier method and used her judgment in doing so. Defendants may cross-examine her about the judgments she made, but their disagreements provide no basis to exclude this computation.

[40] Expert App'x, Dkt. # 1097, at Exh. 5.e, at 2 (Sept. 23, 2020 Errata). *Compare* Expert App'x, Dkt. # 1097, at Exh. 5.a, at 44 (Keyes Rpt.) (8,252 Cabell County OUD cases in 2018), *with* App'x, Dkt. # 1097, at Exh. 5.a, Davies Declaration ¶ 8 (7,627 Cabell County OUD cases in 2020). At the supplemental deposition of October 30, 2020, Defense Counsel's inquiry suggests a line of attack on the grounds that Dr. Davies' figures were somehow inconsistent with those resulting from Dr. Keyes' methodology. As Dr. Keyes pointed out, such purported inconsistency was the result of "cherry-pick[ing] one year" of data, rather than looking at the overall data set. Exh. D, Keyes Dep. 127:18. In any case, such an argument would go to the weight of Dr. Keyes' testimony, not its admissibility.

[41] Expert App'x, Dkt. # 1097, at Exh. 5.a, at 4-5, 44 (Keyes Rpt.).

[42] Exh. H, Rahilly-Tierney Dep. 57:6-9; 73:16-24; 183:9-21.

B. Dr. Keyes' Used a Reliable Methodology to Determine the Appropriate Multiplier for Deaths Involving Fentanyl

Defendants argue that Dr. Keyes incorrectly computed the multiplier for deaths involving fentanyl after 2012.[43] As described above, Dr. Keyes used the known number of overdose deaths and the known rate of death per 100,000 opioid users to compute the total number of persons in the Cabell Huntington Community suffering from OUD. Dr. Keyes applied an adjustment to the known rate of death among users prior to 2013, to account for the higher death rate of the illicit fentanyl that began appearing in approximately 2013. In order to make this adjustment, Dr. Keyes relied on literature showing that the overdose rate due to heroin and synthetic non-methadone opioids increased by a factor of three from 2011 to 2015. For the period up through 2012, Dr. Keyes used a multiplier factor of .52; for the period 2013-2018, Dr. Keyes used a multiplier of 1.5, which is approximately three times the multiplier she used for the earlier period. Applying these multipliers to the known number of overdose deaths through 2018, Dr. Keyes was able to estimate the number of persons with OUD.

Defendants argue that the multiplier would have been higher had Dr. Keyes based it on the rate of overdose deaths from 2011-2018, rather than on the shorter period from 2011-2015. To dress this up as a methodological challenge, Defendants claim that Dr. Keyes ignored the most recent data in making her computation. This is not so. Applying well-established epidemiological principles, Dr. Keyes selected the most relevant time period to determine how to account for the change that occurred in 2013 with the introduction of illicit fentanyl.

As Dr. Keyes explained at her deposition, the period 2011-2015 was the appropriate period to consider in selecting the adjustment because it is a standard epidemiological practice, in dealing with an "interrupted time series"—that is, a change in conditions—to use a small

[43] Def. Mem. at 12-15.

window to bracket the event that brought about the change, in this case, the introduction of illicit fentanyl. *See* Ex. C, Keyes Dep. 331:10-332:14, 318:5-19. Thus, Dr. Keyes considered a time period shortly before and shortly afterwards in order to assess the effect of the change. *Id.* The point is to isolate the changes due to the event from other kinds of changes. In this case, to the extent that heroin use itself increased after 2015, consideration of the rate of overdose deaths in the period 2015-2018 would have conflated the factor Dr. Keyes was trying to assess – increased lethality – with increased use that occurred during that period. Put another way, the increase in deaths after 2015 wasn't necessarily because fentanyl was becoming more lethal; it was because fentanyl use was becoming more common.[44] And yet the purpose of this portion of Dr. Keyes' analysis was to estimate the rate of death among users, not the increase in the number of users. Use of the later data thus would have produced a multiplier factor that was *less* accurate, even though it was based on more "recent" data, because the longer time period would have shifted the focus away from the change that occurred in 2013 with the introduction of illicit fentanyl.

Defendants provide no expert support for their contention that use of later data would produce a more accurate multiplier. No epidemiologist opines that Dr. Keyes selected the wrong multiplier or used the wrong methodology to select the one she used, or that use of recent data is

[44] Plaintiffs are aware that carfentanil, one of numerous "fentanyl analogs" ((FAs) that appeared both before and after 2015, is substantially more lethal than fentanyl itself, and that occasional contamination of the heroin supply with carfentanil resulted in a cluster of overdose reports. However, other FAs are actually *less* lethal than fentanyl, such that their appearance in the supply would have lowered, rather than raised, the rate of overdose deaths compared to fentanyl itself. *See, e.g.*, Exh. I, Wilde, et al., *Metabolic Pathways and Potencies of New Fentanyl Analogs*, FRONT. PHARMACOL., https://doi.org/10.3389/fphar.2019.00238 (2019). For example, Table 1 of that article lists butyrfentanyl, an FA with a potency between 0.03 and 0.13 that of fentanyl, that is, between approximately *8 and 33 times less lethal than fentanyl*. There is no evidence that FAs were, in total, more lethal than fentanyl itself. Dr. Keyes was therefore justified in applying an "average" toxicity of fentanyl and its FAs (Exh. C, Keyes Dep. at 324:6-325:1), and any challenge to its validity would go to the weight of the opinion and not its admissibility.

a helpful way to analyze an interrupted time series. Instead, Defendants rely what they believe to be common sense: that more recent data is always better. But lawyers are not epidemiologists and, depending on the purpose for which it is used, in epidemiology the most recent data is not always better. Dr. Keyes' testimony on this point stands unrefuted.

Defendants also ignore that Dr. Keyes validated the multiplier she selected by comparing the resulting computation of persons with OUD with facts known on the ground as to the number of person diagnosed with OUD in the Community. Using her multiplier, Dr. Keyes estimated "that there are approximately 8,252 individuals who have OUD in Cabell County, who may be in need of treatment services." Expert App'x, Dkt. # 1097, at Exh. 5.a, at 42 (Keyes Rpt.) Recognizing that this number is an estimate, Dr. Keyes applied a "confidence interval" to compute a "plausible range of the number of individuals who have OUD as 8,186 to 8,309," which she calculated "indicates that the prevalence of OUD in Cabell County is approximately 8.9%." *Id.* at 42-43. She then compared this number to data collected and analyzed by Todd Davies, the Associate Director of Research Development in the Division of Addiction Sciences at Marshall University on the estimated prevalence of OUD in the Cabell Huntington Community. This data showed that:

> a total number of 7,627 current, unique individuals have been diagnosed with OUD by the Cabell Huntington Hospital or Marshall Health Clinics, with addresses filtered to identify only those within Cabell County and the City of Huntington. These diagnoses are an underestimate of the total OUD population given that they represent those that came to clinical attention.

Expert App'x, Dkt. # 1097, at Exh. 5.e, at 2 (Sept. 23, 2020 Errata). With at least 7,627 known and diagnosed cases of OUD in the Cabell Huntington Community, the number of actual persons with this disorder who may be in need of treatment services cannot be less than this, and, as Dr. Keyes points out, is surely higher, because Dr. Davies' data captures only those cases of OUD that came to clinical attention. Because the multiplier used in Dr. Keyes' computation is

inversely proportional to the number of OUD sufferers—the higher the rate at which they die, the lower the number of total sufferers can be inferred from a known number of deaths—use of any significantly higher multiplier (as Defendants suggest would be appropriate) would result in an estimate of OUD sufferers that is less than the actual number of known cases. Dr. Keyes used a sound methodology, including a cross-check with current known facts, to arrive at her estimate of OUD suffers. Defendants provide no basis to exclude that estimate.

CONCLUSION

For the foregoing reasons, this Court should deny in its entirety the Motion to Exclude Testimony of Katherine Keyes, Ph.D.

Dated: November 12, 2020

Respectfully submitted,

THE CITY OF HUNTINGTON

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CERTIFICATE OF SERVICE

I certify that on November 12, 2020, a copy of the foregoing was filed electronically. Notice of this filing will be sent to all parties by operation of the Court's electronic filing system. Parties may access this filing through the Court's system. This filing will also be served on all parties by email to: Track2OpioidDefendants@ReedSmith.com and mdl2804discovery@motleyrice.com.

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